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THE DEVELOPMENT OF IDEAS CONCERNING THE CONDUCTION SYSTEM OF THE HEART

by

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IN a profession as rich in proud tradition as medicine is, it is not only an honour but a special privilege to participate in any commemoration of our heroes. Robert Campbell was clearly one of these, a man who combined in an exemplary way the skill and compassion of his professional work with an abiding love of scholarship and culture. In his own Campbell Oration just over 20 years ago, Dixon Boyd recalled him thus " . . . . a successful and busy surgeon who read Shakespeare in a tram-car, and read him with critical and sensitive attention".[1]

Unsurprisingly, Robert Campbell is remembered especially as a teacher of surpassing talent, including some time spent as a demonstrator of anatomy. In teaching the medical students here in Belfast he listed as his first principle: "The basis of clinical work should rest on a sound knowledge of anatomy and physiology".[2] It is a principle to which I wholeheartedly subscribe, but I fear that one part of it has become an unwanted stepchild in many medical schools.

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For reasons that are not particularly clear to me, most medical students and many physicians have lost interest in anatomy. During the period of special turmoil among students the world over in the 1960's, there was serious talk of dropping anatomy from the medical curriculum, said to be a subject of dubious "relevance", a magic word of the time. Perhaps naively, I breathe a sigh of relief that this sort of frenzied insanity seems to have waned.

Critics of anatomy in the curriculum remind me of the exchange between Robert Hutchins of the University of Chicago and a reporter who asked "Do you still teach communism at the University?", to which he replied "Yes, and cancer at the medical school".

To be sure, some of the criticism of anatomy is warranted, for the work of some anatomists has not kept about it that air of freshness which is just essential for effective teaching. It is so unnecessary for such teaching to be stale. When asked "The structure of the body hasn't changed much since Vesalius, has it?", Lactantius is said to have replied "No. Neither has the atomic nucleus".[3]

In his presidential address before the American Association of Anatomists Don Fawcett[4] remarked "It is debatable whether the greenish hue of our image is the fine natural patina that comes with age and exposure or whether it is an incipient gangrene". Fawcett then particularly deplored the lack of precision today in photomicrography, whether of the light microscopic image or that made with electrons, leading to a regrettable and too ready acceptance of pictures out of focus, badly printed, or otherwise poorly presented. It is errant nonsense, he emphasized, to claim that lack of attention to detail is any more tolerable for presenting anatomical data than lack of statistical validity is in physiology or biochemistry. A sloppy photomicrograph is not just an offence to the senses, it betrays sloppy thinking.

Having microscopy as one of my own research interests, I am particularly sensitive to Fawcett's message. In an advertisement commenting upon a course to be offered on photomicrography by the New York Microscopical Society (founded in 1877) jointly with the Royal Microscopical Society (founded in 1839), the Kodak Company explained that whereas microscopy was once considered an academic discipline on its own, today one is expected to learn all about it from the instruction booklet left by a sales representative, as if a microscope were more like an electric toaster than a French horn.

Sir Arthur Keith, of whom I will speak more later, thought that his failure to find an AV (atrioventricular) conduction system in the bird's heart was because of his own faulty microscopic technique, adding that he had always envied masters of such technique almost as much as he envied his friends who could hold free converse in foreign languages.[5]

Of course, defending anatomy in Belfast may be the penultimate form of coals for Newcastle, for your own Thomas Walmsley was not only himself one of the great cardiac anatomists but he taught and inspired a generation of other anatomists who went on to distinguished careers throughout Great Britain, one especially notable one being Dixon Boyd, late of Cambridge. On a more personal note, my own introduction to Belfast was by way of anatomical collaborative studies, first with your Vice Chancellor Peter Froggatt and later and continuing with your State

Pathologist, Professor Thomas K. Marshall. These have been experiences remarkable for me not only because of their intellectual stimulation but no less for the lasting friendships which I have come to cherish.

From my Belfast collaborative studies, as well as related ones before and since, my interest has been inescapably drawn to the historical development of our knowledge concerning the conduction system of the heart. Man has been so fascinated by the heart beat throughout recorded history—witness the ritual excision of human hearts in Aztec sacrifices, a people who incidentally left no written history—that it is difficult to know just where to begin, or whom to accredit. What I shall do with your indulgence is to recite a litany of heroes personally chosen for what their work has meant for me, and take the liberty of interspersing a few of my own observations.

It is no exaggeration to say for electrical activity of the heart, as can be said for all of biology or even all of science, that the growth of our knowledge in the past few decades transcends all prior accumulated information, often by several orders of magnitude. And yet, the very foundation for what we presently know and for what we still seek to know about this subject was carefully and precisely laid in the astonishingly short period between 1893 and 1907. Those who then opened the windows to horizons which are still new were Arthur Keith, Wilhelm His, Jr. and Sunao Tawara. Earlier contributions from Johannes Purkinje were recognized entirely in retrospect and, with no disrespect intended, afford an almost comic relief in the drama of this story.

Before proceeding to some description of these special men's works, every one of which, incidentally, dealt with *histological* anatomy, it may be well briefly to examine the temper of those times. The intellectual psychological ferment of the late nineteenth century indisputably had a powerful influence on what may be seen as a solar flare of science.

For about the second half of the 1800's there was a growing and eventually furious scientific debate between those who had held that the process of cardiac excitation spreading from the atria to the ventricles was by way of nerves and those who said it was muscle. This argument between neurogenic and myogenic theorists neared its peak intensity in 1890. Then as those pioneers to whom I have already referred began to publish their work, a second force came into play, what may be called scientific chauvinism, a trait more powerful and pervasive than most of us would enjoy admitting. Remember that my cast of characters includes a Japanese scientist working in Germany, a multi-national German in Berlin, a modest Englishman working with a medical student neighbour, and a Czechoslovakian physiologist who had dabbled in everything.

There are several reasons why I will begin with Sir Arthur Keith.[6] From all accounts Keith (Figure 1) was a thoroughly likeable, honest and meticulously careful scientist who had that special ability to bring bits and pieces of knowledge together into a wondrous whole. He is also, with young Martin Flack, indisputably the discoverer of the sinus node, where the heart beat normally originates. Finally, of all elements of the system for impulse formation and conduction within the heart, it is the sinus node which I confess has long been the most fascinating to me. I might digress to add that my introduction (by correspondence) to J. Dixon Boyd, one of

Figure 1.
Sir Arthur Keith in 1912 at age 46.

your most illustrious alumni, came because of my defense for Thomas Walmsley's simpler and more accurate term "sinus node" instead of the more cumbersome and anatomically misleading sinoatrial or sinoauricular node. Boyd applauded my decision to buck what was then a trend, and recalled from his own memory how strongly Walmsley, his teacher here in Belfast, had felt about the same matter.

Just after the turn of the century, Keith and his wife were renting a farm house in Kent when he received a letter from Sir James MacKenzie informing him of Tawara's discovery of the AV conducting system. MacKenzie then began sending Keith hearts from cases of cardiac irregularities to see if there was a pathological basis. Even today one is mystified about what it was that MacKenzie suspected, given that electrocardiography was just being born and the sinus node had not even yet been discovered. Undaunted, Keith began to make many histological sections and was soon intrigued by a localized density of richly innervated right atrial tissue at the junction of the sulcus terminalis and superior vena cava. Uncertain of its functional significance and unaware of Tawara's "knoten" at the time, he only made a mental note of this curiosity.

In the long summer vacation of 1906 Keith, having converted the study of his farm house into a histological laboratory, assigned to his medical student neighbour, young Martin Flack, the examination of a variety of mammalian hearts. Returning one hot afternoon from a bicycle ride with his wife, Keith found Flack all excited with what he had found from serial sections of the heart of a mole. Because he remembered seeing a similar structure in the human hearts from MacKenzie, Keith set to work with young Flack to examine the same location in a remarkable array of species. There were fish, amphibia, reptiles, birds, and the following mammals: mole, porpoise, kangaroo, whale, shrew, ram, pig, horse, fetal gibbon and two human embryos. However, it was the memory of what he had seen in MacKenzie's hearts, and subsequently, knowledge of the similarity of this newly found structure to Tawara's knoten which led Keith to postulate (correctly) that the sinus node was the origin of the heart beat.[7]

Although Keith had gone to Leipzig for a few months in 1895, thinking to study with His the elder, who was an outstanding embryologist of the day, he did not stay in Leipzig. Nor is there any record to my knowledge that he ever worked with His the younger or with Tawara, although it seems inconceivable that they did not eventually meet or at least correspond.

Less familiar to most than the 1907 work on the sinus node[7] is another report by Keith and Flack published the previous year.[8] Although the title of the 1906 paper referred to the AV bundle, this remarkably lucid description also dealt with the AV node, the bundle branches and the Purkinje system. It was a complete and enthusiastic confirmation of Tawara's recently published studies,[9] which Keith very obviously admired. It also went a long way toward producing an intelligible synthesis of a concept for a cardiac conduction system, a concept crowned the next year when the actual source of the cardiac impulse was first reported.[7]

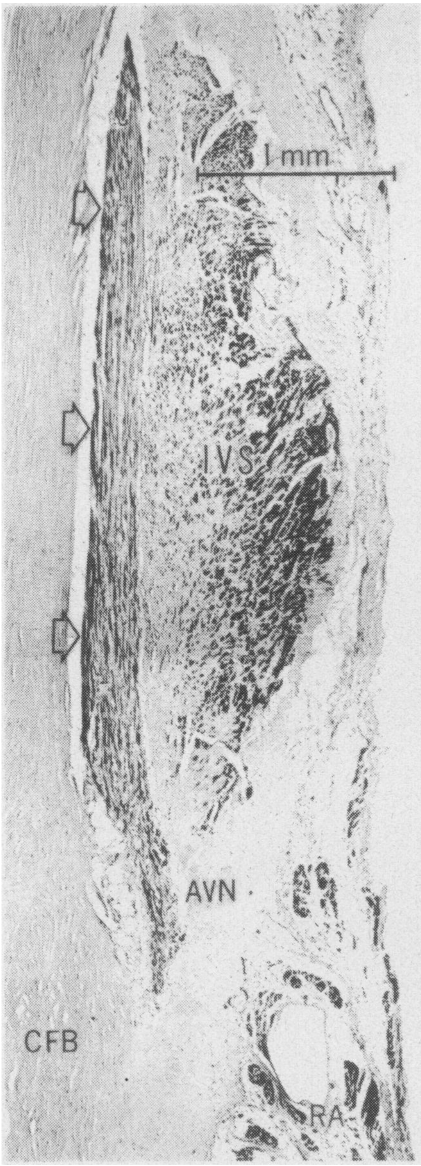
Keith did not stay with the sinus node nor the conduction system, and I am not sure why. He was a man of very broad interests, beginning with three early years in Siam where he studied botanical specimens and anthropology (monkeys), and where he nearly died of falciparum malaria. His life work on human embryology and anatomy produced an admirable book which went through six editions.[10] One vexing experience was his tangential involvement in the controversy about the skull of Piltdown man,[6] an issue in which he was ultimately proved to be correct, but he was too gentle a man to battle with those who were more vocal but wrong. For his exceptionally accurate anatomical discovery of the sinus node and correct appreciation of its significance, for his generous admiration and quick confirmation of the work of Tawara and his early and thorough expostulation of its importance, and for a full life of quiet scholarship, Keith ranks very high in my own pantheon of heroes in medical science.

Sunao Tawara (Figure 2) was born in Oita prefecture in Japan in 1873. After graduating *summa cum laude* from Tokyo University as a doctor of medicine in 1901, he was accepted in Marburg, Germany, in 1903 to study with Ludwig Aschoff. From those three years in Marburg he published in 1906 his monumental work, "Das Reizleitungssystem des Saugetierherzens", with a foreword by Aschoff.[9] As was quickly grasped by Keith and others, including his German mentor (Aschoff), Tawara's book was not only a masterly distillation of his own meticulous work but a brilliant synthesis of existing knowledge about the conduction system into an integrated whole. The only major element missing was the sinus node, and Keith and Flack soon gave us that, in part being guided by knowing about Tawara's "AV knoten".

Tawara knew of the important report by His in 1893, as did Keith and other contemporary students of the subject. But Tawara was the first to describe how the His bundle was expanded at its proximal end to form a meshwork of slender fibres compacted together like a knot or node

Figure 2.
Sunao Tawara of Japan.

(Figures 3 and 4). In addition to his generally recognized priority for discovery of the AV node, he probably also deserves credit for first recognizing that the His bundle divided into consistent right and left branches comprised of fibres such as those originally described by Purkinje in 1839[11] and 1845.[12] Tawara correctly interpreted that the AV node, His bundle and its branches together formed a system whereby all electrical impulse propagated from the atria to the ventricles in the mammalian heart, including that of man. Tawara's histological illustrations are still as accurate



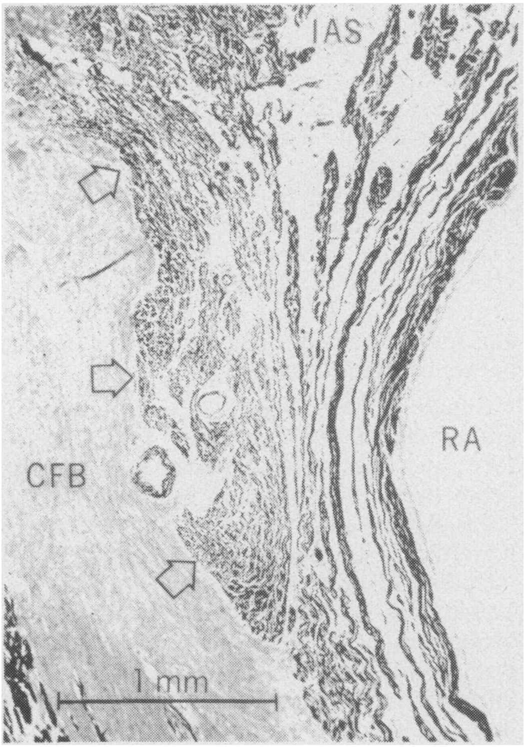


Figure 3 (left).
This horizontal plane section of a human His bundle (three open arrows) shows its proximal expansion into an AV node (AVN). CFB is central fibrous body, RA right atrium and IVS the crest of the interventricular septum. Goldner trichrome stain here and in all other photomicrographs unless otherwise indicated. All magnifications are indicated with reference bars.

Figure 4 (above).
This frontal plane section is made through the AV node (three open arrows) of a normal human heart.. RA indicates the chamber of the right atrium.and IAS is interatrial septum.

as they are beautiful, but it was his original and imaginative description of just how the system was organized and exactly how it worked that is equally beautiful.

When Tawara returned to Japan in 1906, he served as associate professor of pathology first at Kyoto and then Fukuoka medical schools. In 1908 his alma mater in Tokyo awarded him a special degree in recognition of his research, and in 1910 he became professor of pathology at Kyushu University, where he remained until his retirement in 1930. In 1914 he received the Japan Academy prize for his work on the cardiac conduction system, but until his death in 1952 he—like Keith before him—did not pursue other aspects of his great original contribution.

Wilhelm His, Jr. (Figure 5) was the worthy son of a famous anatomist. Even in those days, academicians were a peripatetic lot and the young His attended the universities of Leipzig, Strasbourg, Bern and Geneva. He was not only a capable clinician but also a talented violinist and painter. Although he studied gout and certain types of fever, his most lasting contribution was the correct description of the AV bundle which now bears his name.[13] However, while the description by Wilhelm His is almost certainly the first that can be judged to be anatomically and physiologically correct, there was for some time considerable dispute in priority, in part because scientific chauvinism reared its ugly head. There was also fierce and derogatory criticism from proponents of the neurogenic theory of conduction who properly surmised that His's discovery could destroy their raison d'etre.

An early challenge to His's priority came from A. F. Stanley Kent, accompanied by those who wanted to champion British priority for the discovery. It is true that in the same year as His (1893), Kent independently described findings supported myogenic rather than neurogenic conduction.[14] There seems little doubt that Kent did not know of His's work, nor His of Kent's. But there the similarities end. What Stanley Kent actually said[14] was that there were normally multiple AV connections in the mammalian heart, most of which were over the lateral aspects of the AV valve rings, thus claiming to confirm what Gaskell[15] and others had found in the tortoise. Although Kent did mention the septal AV connections in his 1893 paper, he attached no particular significance to them and in later works[16, 17] conspicuously ignored what is today known as the His bundle. In essence, Kent repeated the equally vague and much earlier descriptions of Paladino,[18] an Italian scientist who at a later time[19] also challenged His's priority.

Following Stanley Kent's initial reports in 1893 and 1984, he did not publish further on the subject for 20 years, a

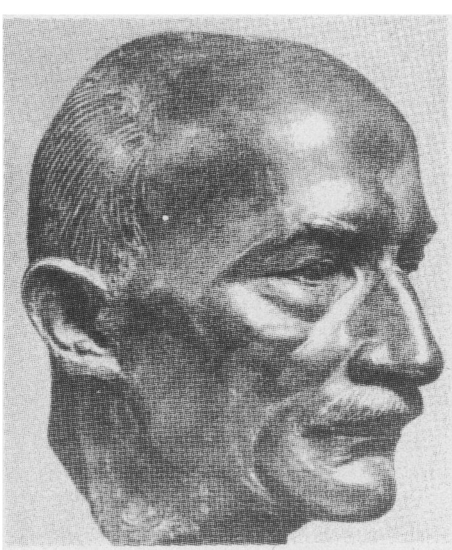


Figure 5.
Photograph of a sculpture of Wilhelm His, Jr.

period during which the work of His was being widely accepted both clinically and experimentally. Finally, in 1913 and 1914 Kent[20, 21] presented a series of reports, most of them in the form of brief abstracts, which purported to prove that AV conduction did not utilize the bundle described by His. He even described an experiment in which he claimed to have severed all AV connections except a right lateral AV strip without significantly disturbing the heart beat. In 1953 Frau, Maggi and Agostini repeated that experiment using the same species (rat) and proved that Kent was wrong.[22]

For interpreting Kent's work in context and for understanding his persistence, Öhnell[23] has suggested that anyone historically interested in the matter should carefully examine the statements available in the reports of two British committees specifically charged with evaluating the question of functionally significant AV connections other than the His bundle. Both committees were organized under the auspices of the British Association for Advancement of Science, one in 1894[24] and the other in 1915,[25] thus corresponding to Kent's earliest and latest work. Somewhat surprisingly, Kent was appointed secretary of both committees and must be presumed to have written the reports, hardly an arrangement to inspire confidence in their scientific objectivity. Sherrington was a member both times, chairing the 1915 meeting. As might be expected, both reports fully supported Kent's position, even using first person pronouns.

One must conclude in truth that Kent saw or found little if anything not already described by Paladino and Gaskell, and even by Henle in 1968,[26] and that he not only failed to grasp the special significance of what he saw in the septa but that he misinterpreted his findings. In his own later biographical recollections of the historical events, Wilhelm His[27] comprehensively compares his own observations and interpretations with those of his challengers, having the advantage of over a half century of subsequent perspective. Now approaching (in about another decade) the centennial anniversary of the report by His, we can only conclude that the true priority is no longer in any reasonable dispute and properly belongs to Wilhelm His, Jr.

Johannes Evangelista Purkinje (Figure 6) is quite a different story and offers an interesting lesson in the nebulous origin of eponymous fame. Born in 1787 the son of Bohemian peasants, Purkinje gave early evidence of being a successful striver. He became a linguist not only skilled in Czech, German and Latin, but he could also speak French, English, Russian, Polish, Greek, Italian, Hungarian, Serbian, Lithuanian and Danish. As a multilingual friend of mine once asked, "I wonder what language he dreams in?" Purkinje was additionally a poet, writing odes and

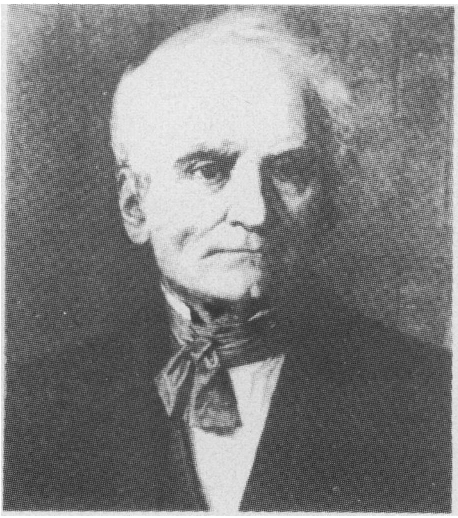


Figure 6.
A portrait of J. E. Purkinje (or Purkynê).

lyrics, but he was a terrible lecturer and hated that form of teaching. Few knew or know just how to spell his patronym, which is found in at least nine different versions in the literature.[28]

There must be very few others in medical history with such a broad range of meaningful scientific interests and contributions. Purkinje not only invented or established the principles for the ophthalmoscope, the spirometer and the hearing aid, but he discovered new aspects of the psychology of dreams, how to do capillary microscopy in vivo, how nerves influence the secretion of gastric acid, and what the germinal vesicle of an egg was. Purkinje was the first systematically to study dermatoglyphics, that arcane science of fingerprints, and he coined the word "protoplasm".

Today his name remains enshrined in anatomy because of Purkinje cells in the cerebellum and Purkinje fibres in the endocardium of the heart. The endocardial fibres were discovered in ungulates, where they are indeed conspicuous structures, but Purkinje was unable to find them in the rabbit, dog or man. He was not even sure what they were, suggesting that they be classified as cartilage. So little was thought of any functional significance for Purkinje fibres that an 1899 biographer[29] does not even mention them among Purkinje's contributions. That may have been a judgement call, but Tawara changed things (and immortalized the Czech physiologist, at least in cardiology) when he chose to discuss Purkinje fibres as the ventricular terminus of specialized conduction tissue in the heart. There has long been and still remains a great deal of confusion and obscurantism about Purkinje fibres. The Czech physiologist (anatomist?) described them as fibres rather than cells. And fibres rather than cells was indeed the prevailing wisdom about the heart until the 1950's and the dawn of electron microscopy. It was only then that the true nature of the intercalated disc as an intercellular junctional membrane became clear,[30] and the myocardium was proven not to be an anatomic syncytium. Paradoxically, very recent studies with freeze-fracture and similar techniques for scanning electron microscopy have re-opened the question, at least to the point of suggesting that the myocardium may function as an excitable syncytium, even if this is not anatomically so.

But there is even greater disagreement as to how to define a cardiac Purkinje cell. Are they present in the human heart (Figure 7), where Purkinje could not find them, or only in ungulates where he did? Are Purkinje cells also present in the atria or only in the bundle branches of the ventricles? Physiologists would have us define them by rapid conduction velocity, reflecting one property with which physiologists are more comfortable, and it is true that conduction is rapid most places where there are Purkinje cells. For example, cells of the Purkinje type are distinctly present in the human atria, particularly in sites of preferential atrial conduction.[31, 32] While these pathways of preferential atrial conduction are not isolated or anatomically shielded as the ventricular bundle branches are, at least in their initial course, regional shielding or non-shielding of a multicellular area is hardly a basis to disqualify any proposed cellular definition of atrial myocytes. Furthermore, arguments as to whether the atrial cells are "specialized" (or not) nearly always take as a necessary definition that specialized means rapid conduction, whereas there are other equally important electrophysiological specializations, as well as anatomical ones.

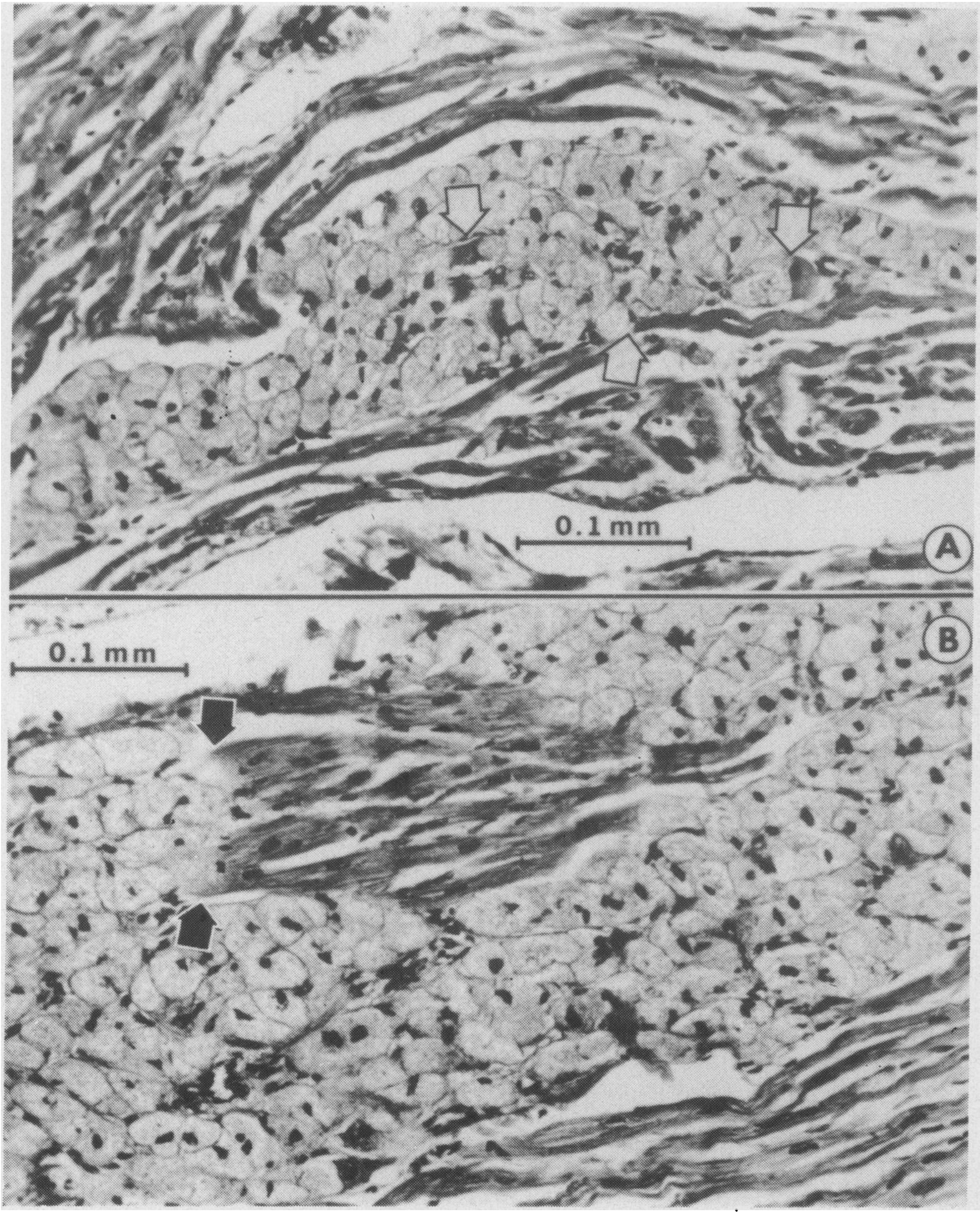


Figure 7.

Human Purkinje cells are clearly visible in these two photomicrographs of a Purkinje cell tumour. The open arrows in A and the black arrows in B mark points of junction with ordinary working myocardial cells.

One electrophysiological specialization in the heart is the property of automaticity, and Purkinje "strands" are a favourite tissue for physiologists to study automaticity. And yet, most such studies ignore three fundamental points. First, Purkinje cells seem specialized for rapid conduction whereas conduction in sites of normal automaticity (such as the sinus node) is always very slow. Second, the only normal automatic centre and primary pacemaker in the heart, the sinus node, does contain specialized cells, but they are not Purkinje cells, differing markedly both by anatomic and physiologic definition. In fact, there are no Purkinje cells in the sinus node. Third, the cells in Purkinje strands, whether studied in vitro[33] or in vivo[34] are not spontaneously automatic under *normal* conditions, and *induced* automaticity differs significantly from that of the sinus node when biochemically defined.[35]

Here we are, nearly a century and a half after Purkinje's discovery, still puzzled about his cells and what they do and exactly where they all are in the heart and how much significance to attach to their species difference. But I believe if Purkinje himself were to judge carefully where he made his major contributions, it would have to be in the science of vision. Even there, however, his irrepressible curiosity ranged widely, and was nearly the cause of his death. Because of visual complaints by his patients (he remained a physician) who had been advised to use digitalis or belladonna, Purkinje undertook experiments upon himself to examine the nature of these puzzling symptoms. Although he subsequently provided vivid descriptions of scintillating scotomata and colour aberrations, as well as nausea and cardiac arrhythmias, after ingesting a huge amount of digitalis,[36] he was lucky to survive. As an interesting recently proposed side light of history, new evidence[37] suggests that some of Vincent van Gogh's most remarkable paintings, including the popular "Starry Night", were but the visual aberrations produced by toxic amounts of digitalis.

Whatever his many scientific contributions may ultimately mean, Purkinje was clearly a master of academic gamesmanship. Both Schiller and Goethe were his literary inspirations, but Goethe's personal influence and recommendation (he was then 74) were additionally instrumental in Purkinje's appointment to the chair in physiology at Breslau at the age of 36. The microscope essential in many of Purkinje's studies was denied him by the university (it cost $50) so he bought one himself. At a time when physiology was being taught by anatomists, Purkinje not only concentrated his efforts (anatomical as well as physiological) in a department of physiology, but he procured separate housing and eventually an institute, a model later to be emulated by many major medical centres in Germany and elsewhere. Some also say that his imagination and creativity declined in inverse proportion to his administrative and bureaucratic triumphs, and if true, it would certainly not be the first or last such lesson from medical history. In his later years he became a fervid Slavic nationalist, eventually dying full of years at the age of 82.

Keith, Tawara, His and Purkinje are names written large in the annals of our knowledge about the conduction system. While Purkinje was the only physiologist of the group, he never studied the function of his fibres, no doubt in part because neither appropriate electrophysiological concepts nor any suitable tools for their study were available in his time. Wilhelm His not only recognized the functional significance of his bundle but correctly anticipated that lesions there could account for Stokes-Adams attacks, expressing disappointment in his final years that he never had the opportunity to conduct an appropriate clinicopathological correlative study to prove the point, although I am puzzled as to why that should have been. Keith also failed to embark upon physiological studies, perhaps being intimidated by some of the giants already aggressively into the field, but Keith better than most understood the critical intellectual bonds between anatomy and physiology, once emphasizing that William Harvey was fundamentally an anatomist whom the physiologists later stole as their own patron saint. Harvey was of course both an anatomist and a physiologist and undeniably a genius in both fields, as was Purkinje.

Leaving out Purkinje, who was from a different era, why did His, Tawara, and Keith not pursue these logical extensions of their work? Others quickly did. One explanation is surely the invention of Einthoven's electrocardiograph at the start of this century, and the explosive growth of basic and clinical research with it. But many electrocardiographers were eager to seek anatomical correlations, as witness MacKenzie's prescient teasing of Keith's curiosity. Both Keith and Tawara were most comfortable as anatomists and, perhaps due to modesty, did not range far from that field. Wilhelm His may actually have been uncomfortable as an anatomist, living as he did in the shadow of his famous father. But even today there is a perplexing reluctance for most scientists to cross disciplines, a condition which one of my friends aptly describes as "sclerosis of the categories".

If there is a lesson to be learned from this historical view of the work of these four men, it may be that they could have told us more about the conduction system than they did. This is not intended as an irreverent remark but as a tantalizing look at what might have been. Here today and certainly for the future, how can we encourage cross-disciplinary thinking but at the same time escape the spectre of superficiality, thus re-create Renaissance man but not the dilettante?

Is it possible to foster—in today's world of more and more specialization—a greater interest and appreciation of the importance of knowing as much as possible about normal and abnormal structure of the cardiac conduction system, as well as how it works? It would seem to me that one just cannot fully understand how something functions in the absence of knowing just how it is constructed. Many of our worst misconceptions today in both clinical and basic cardiac electrophysiology can be directly traced to the continued prevalence of a shocking ignorance of anatomy.

At the same time I must express grave reservations about the popular approach of team research in science today. Perhaps there is too much to know about some subjects, but it is impossible to know to the fullest *any* subject if only one aspect of it is studied, whether that be its biochemistry, physiology or anatomy. When separate investigators who can hardly understand each other's scientific language, much less the nuances, come to work together, we do not get a hypothetical blending of the best of several worlds. The predictable product is a Tower of babel. Second-hand knowledge, whether gained from books or from a valued colleague, can stimulate, excite and sometimes explain, but it is always a poor substitute for learning from personal experience.

Permit me now some predictions about future research on the anatomy of the cardiac conduction system. I have already emphasized the need for more cross-

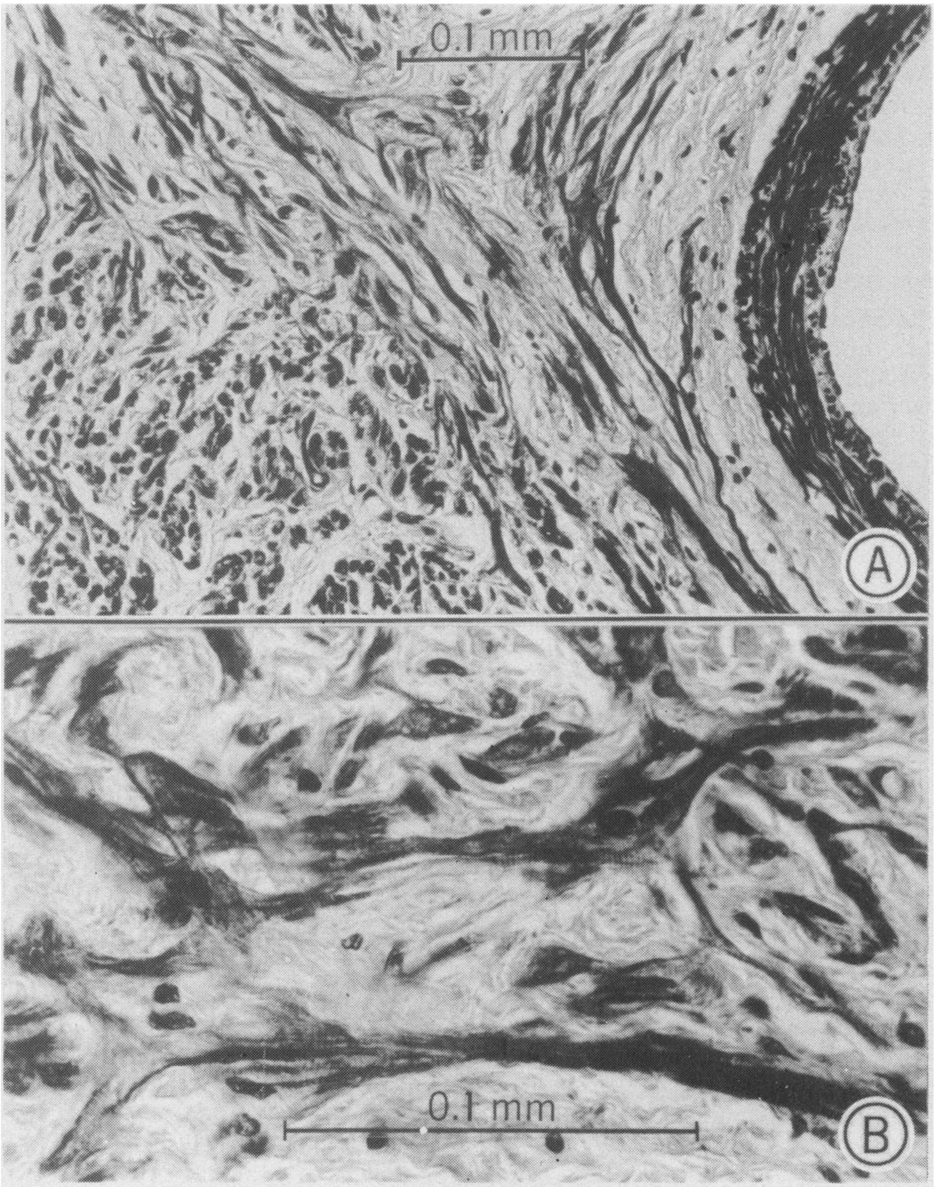


Figure 8.

The variety of cells typical of the human sinus node is illustrated here at two magnifications. All tissue shown is sinus node, and a portion of the central artery is seen at the right margin of A. Collagen is light grey, and contains an interweaving meshwork of darker nodal cells of two principal kinds: a slender one containing numerous myofibrils (transitional cells) and an ovoid pale cell with very few intracellular organelles or myofibrils (P cell). See also Figure 9.

disciplinary work, not by teams but by individuals. Or as any medical student might put it, where is Purkinje now that we need him?

In anatomy particularly there is likely to be some redirection, a change from reductionist to holistic research. Don Fawcett admitted that vigorous exploration of the cellular and molecular levels of organization can accelerate our understanding in the short term, but then cautioned: "the frenetic effort to reduce all biology and medicine to physics and chemistry loses sight of the fact that our ultimate concern is the understanding of the whole organism. Eventually we will have to work back up from the molecular level and from the simplest organisms to higher levels of organization and to higher animals".[4] And dare I add, to man himself.

Let me illustrate this point from personal experience with the sinus node of Keith and Flack. There are remarkably important differences both anatomically and physiologically between the human sinus node[38-40] and that of the bat,[41] rabbit,[42] cow[43] and dog[44] but few pay attention to these differences. Furthermore, there is a variety of totally different cells within the sinus node (Figures 8 and 9), it has an intriguing centrally located artery (especially in man and the dog), and its function is profoundly influenced by the richly abundant nerves there.[45, 46] There is no way fully to understand sinus rhythm of the heart by studying separate cells in the sinus node without realizing how they relate to each other. There is no way to explain nodal function without carefully considering its innervation or its conspicuously prominent central artery. In short, intracellular fine structure and transmembrane flux of ions are all very fine to know, but one is still faced with the inescapable fact that the sinus

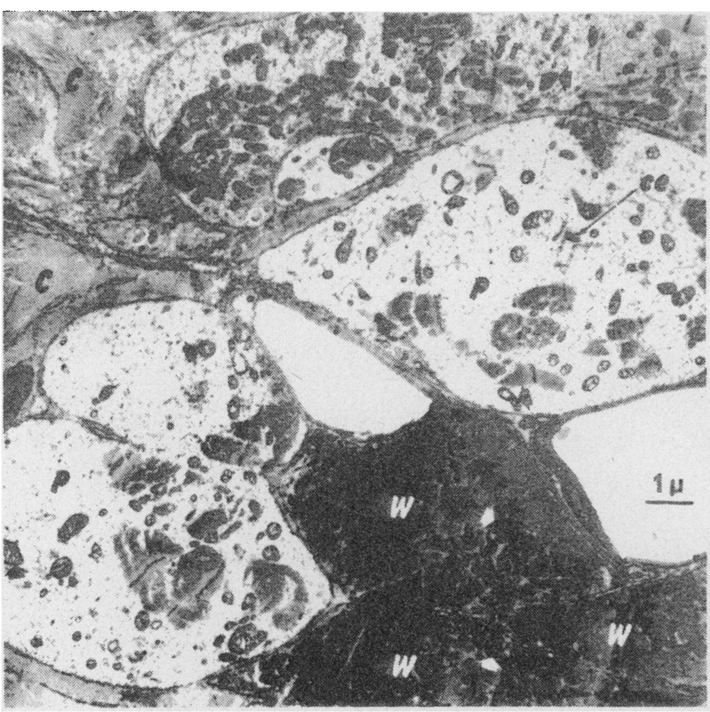


Figure 9.
This electron micrograph of canine sinus node was prepared from a specimen fixed in vivo by selective perfusion with glutaraldehyde. The contrasting appearance of P cells (P), transitional cells (Tr) and working myocardium (W) is demonstrated. C marks collagen fibrils and ce is a centriole. Small arrows indicate mitochondria which differ in complexity in the different types of cells.

node is a complex and heterogeneous multicellular biologic unit, the ultimate integrated function of which in vivo is markedly dependent upon its innervation and blood supply. Someone has said that what we truly need is more complexifiers and fewer simplifiers. Albert Einstein put it this way: "Everything should be as simple as it can be, but not simpler".

Occasionally, and not often, I am glad to say, I hear remarks that Keith and Flack's sinus node was only an anatomical curiosity until the physiologists "proved" its functional importance. Let me remind those making such remarks that the work of Gaskell and other stellar physiologists was largely at an impasse until the anatomical discoveries of a muscular bundle connecting atria to the ventricles, and of a peculiar mass of twisted, richly innervated fibres at the atriocaval junction, a newly recognized structure which could immediately be suspected to be the origin of the heart beat. It was only after those anatomical discoveries that knowledge about cardiac rhythm and conduction took a quantum leap forward.

Science will surely be better served if those in both fields heeded Robert Campbell's first dictum of medical teaching and more readily admitted their need for each other. Anatomists must be more ready and willing to conduct physiological studies. Physiologists just as obviously need to know, personally and first-hand, more about the anatomical structure of any tissue they are studying. Breaching these artificial barriers between intellectual disciplines should not be looked upon as a scientific sin but as a triumph for truth.

For those misguided sceptics who have been too ready with an epitaph for anatomy, listen to a small homily from my friend and fellow student of the sinus node, Reginald Hudson.[47] "If you are like me, you will often feel bewildered by the contradictory findings about medical mysteries, emanating not only from conscientious investigation but also from the sort of second-hand research done by punch-card and computer. May I therefore leave you with this piece of advice. It was given by a sergeant who was instructing a batch of recruits in map-reading. He said "if there is a discrepancy between the map and the ground you can take it as a main rule that it is the ground that is correct!".

A Czech born in Bohemia, a German born in Switzerland, a Japanese working in Germany, and an Englishman born in Scotland, come together in a marvellous international panorama of the anatomical history of the conduction system of the heart. There have been many others of course, and I must apologize if I have omitted any of your own favourites.

Johann Wolfgang von Goethe, Purkinje's intercessionary benefactor, has written: "One ought, every day at least, to hear a little song, read a good poem, see a fine picture, and, if it were possible, to speak a few reasonable words". My own words today are to honour the memory of Robert Campbell, a man whom the German poet's thoughts fit so well.

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